Carbopol 974P

Brand Name: BufferGel
Drug Class: Microbicides

Drug Description

Carbopol 974P, a buffer agent, is an extremely high molecular weight, cross-linked polyacrylic acid and is highly negatively charged, with thousands of ionized carboxyl groups per molecule. These features help prevent transmucosal absorption of the buffer agent. Moreover, a polymeric buffer avoids two related problems: the product will not become hypertonic when high concentrations of buffer material are used, and the polymer will not cause the cytotoxicity that is seen with use of small, absorbable buffers such as acetic or lactic acid. [1] Carbopol 974P polymer is used as a gelling or tableting agent in many pharmaceuticals. [2] It is the major nonaqueous component (5% polymer, 94% water) of BufferGel. Additional constituents of BufferGel are dibasic potassium phosphate, magnesium sulfate, dibasic sodium phosphate, sorbic acid, monobasic sodium phosphate, and disodium EDTA. [3]

HIV/AIDS-Related Uses

Carbopol 974P is a polymer gel that maintains vaginal acidity, possibly impairing or preventing the transmission of HIV and other sexually transmitted diseases (STDs). Carbopol 974P is formulated as a nonirritating vaginal lubricant called BufferGel. BufferGel is being investigated for the prevention of sexual transmission of HIV.[4]

Non-HIV/AIDS-Related Uses

Microbicides are woman-controlled methods of STD protection and therefore do not rely on a partner's use of a condom. In addition to protecting a woman from STDs and pregnancy, it is believed that a man would be protected from STDs if his partner used a microbicide.[5]

Microbicides may be able to block infections of STD pathogens by creating a barrier between the pathogen and the reproductive tract (vagina and cervix) or rectum or by preventing a virus from replicating once it has entered the body. Carbopol 974P may prevent the transmission of numerous STDs, including chlamydia, gonorrhea, human papillomavirus, and herpes simplex virus (HSV)-1 and HSV-2.[6]

A microbicide may be able to prevent unwanted pregnancy by killing sperm; carbopol 974P is also under study as a spermicide to prevent pregnancy.[7]

In a pilot study of 10 women, BufferGel was a moderately effective treatment for bacterial vaginosis.[8]

Pharmacology

Carbopol 974P is a negatively charged, high molecular weight polymer which is not absorbed and can neutralize twice its volume of base buffers, such as semen.[9] Carbopol 974P is formulated to buffer the concentration of free hydrogen ions at 0.1 mM, the level normally found in the vaginal lumen (pH 3.8-4.0). Hydrogen ions are buffered by the carboxyl groups that occur in large quantities on the carbopol 974P polymer.[10]

Carbopol 974P acidifies semen to a pH less than or equal to 5.[11] In vitro, sperm and many STD pathogens are inactivated at a pH less than 5. The reported pH necessary for HIV inactivation is between 4 and 5.8 in different studies.[12]

BufferGel is water based and detergent free and has low osmotic activity. It contains no oil and is compatible with condoms and latex diaphragms.[13]

Adverse Events/Toxicity

In a Phase I clinical trial, BufferGel showed minimal toxicity and was well tolerated, although two-thirds of the participants reported at least one mild or moderate adverse event. The most common adverse events were vaginal itching and irritation. Some symptoms disappeared within 1 hour after application of the product. Vaginal candidiasis and hyperkeratotic lesions required discontinuation of the product in a small percentage of trial participants. Three colposcopic abnormalities were observed, but no cases of epithelial disruption occurred.[14]

Carbopol 974P

Adverse Events/Toxicity (cont.)

An international Phase I clinical trial had similar results. Adverse events were categorized as mild to moderate and included presence of Candida on wet mount, vaginal and vulvar itching or burning after gel insertion or when passing urine, labial rash, lower abdominal pain, and vaginal discharge. Irritation was reported in approximately 25% of women in the study and was generally mild and of short duration. Epithelial abnormalities detected by pelvic exam or colposcopy were uncommon.[15] In both trials, adverse effects of BufferGel were generally self-limiting and readily resolved. Both trials reported a high degree of compliance and acceptability.[16] [17]

In a Phase I clinical trial of penile application of BufferGel, no serious adverse events or urethral inflammation were reported, and adverse event rates were not significantly different from placebo.[18]

Clinical Trials

For information on clinical trials that involve Carbopol 974P, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Carbopol 974P AND HIV Infections.

Dosing Information

Mode of Delivery: Intravaginal.[19]

Dosage Form: Topical gel.[20]

Storage: Store at room temperature.[21]

Chemistry

CAS Number: 151687-96-6[22]

Physical Description: Aqueous gel formulated at pH 3.9 to 4.0 with sufficient buffer capacity to acidify (to pH less than 5) approximately twice its own volume of human semen.[23]

Other Names

Carbopol 974P polymer[24]

Carbopol polymer[25]

Carbomer 974P[26]

Further Reading

Bentley ME, Fullem AM, Tolley EE, Kelly CW, Jogelkar N, Srirak N, Mwafulirwa L, Khumalo-Sakutukwa G, Celentano DD. Acceptability of a microbicide among women and their partners in a 4-country phase I trial. Am J Public Health. 2004 Jul;94(7):1159-64. PMID: 15226137

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Turpin JA. Considerations and development of topical microbicides to inhibit the sexual transmission of HIV. Expert Opin Investig Drugs. 2002 Aug;11(8):1077-97. PMID: 12150703

Manufacturer Information

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Carbopol 974P

Manufacturer Information (cont.)

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

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2. Protocol ID: HPTN 035 - Ver. 2.0, p. 36

3. Protocol ID: HPTN 032 - Ver. 2.0, p. 18

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6. ReProtect LLC - Microbicide Development. Available at: http://www.reprotect.com/microbicide.shtml. Accessed 02/23/05.

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8. J Womens Health (Larchmt) - 2003 Apr;12(3):255-9

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13. ReProtect LLC - Product Information. Available at: http://www.reprotect.com/products.shtml. Accessed 02/23/05.

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